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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/766,863

Applicant(s)

POWELL ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6,7 and 10-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6,7 and 10-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____

DETAILED ACTION

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) filed on September 24, 2003. The request for RCE is accepted and is established with the status of the application as follows:

- a. the filling date of this RCE is established as January 29, 2001;
 - b. Claims 1-3, 6-7, 10-20 are pending. Claims 4-5, 8-9 are cancelled previously.
2. Applicants' response to the earlier office action filed on September 24, 2003 is reconsidered and has been entered.

Response to Arguments

3. The following is the rejection maintained in the previous office action under 35 USC 103(a):

Claims 1-3, 6-7, 10-15, 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (WO 99/37817) and in view of Kamb et al. (USPN. 5,998,136).

Johnson et al. teach a method of identifying the function of a test compound, wherein Johnson et al. disclose that the method comprises (i) providing a plurality of cells, the plurality comprising at least two different cell types and exposing the plurality of cells with a test compound (see page 53, lines 1-60; (ii) measuring expression of one or more genes in the said cell types and comparing the expression of said genes with a reference cell and an alteration in said gene expression indicates the function of said test compounds (see page 53, claim 1, lines 7-15, page 11, lines 3-5). Johnson et al. also teach that the method comprises (i) expression of at least two genes in two different cell types (see page 53, claims 2 and 3) (ii) defines different gene-cell combination as the same gene in two or more host cell types or, two or more different genes in the same host cell type (see page 7, lines 24-31), which indicates more than two cell

types and more than two genes are permissive in the said method which is supported by the results in table 1 of Johnson et al. disclosure (see page 20, table 1, lines 1-4); cells are provided in container (plates) and the cell types consist of HepG2 cells, B-cells, T-cells, astrocytes (see page 27, lines 1-11, page 30, lines 8-10); gene expression greater than or equal to 3-fold was taken as an indication of modulated gene expression by a test compound. (see page 28, lines 19-20); test compound could be a polypeptide (see page 54, claim 14); plurality of cell types were contacted with two or more test compounds (see page 54, claim 12); plurality of cells include mammalian cells from human subjects (see page 39, lines 12-19). Although Johnson et al. teach HepG2 cell type, Johnson et al. did not specifically teach other mammalian cell types listed in the instant claims, that is cell types comprising osteosarcoma, erythroleukemia, monocytic, endothelial, fibroblast, NK-cell, normal osteoblast, normal lung fibroblast.

Kamb teaches a method for identifying test compounds wherein Kamb teaches that the method comprises identifying the function (inhibitory effect) of a test compound on cells and measuring gene expression (see column 34, lines 41-67); the cell types comprise most preferably mammalian cells (see column 35, lines 1-7); Cell types comprise, fibroblast, endothelial, epithelial cell types (see columns 13-14, table 1). Kamb also teaches detection of differential expression using sequence tags and polymerase chain reaction (see column 21, lines 41-67).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Johnson et al. with the method of Kamb which is applicable to select different mammalian cell types because Kamb states that mammalian host cells are more preferable and the compounds identified by screening could be used to prevent diseases such as cancer, neurodegenerative, immunological or

inflammatory diseases” (see column 35, lines 1-7, column 43, lines 39-57). An ordinary practitioner would have been motivated to combine the method of Johnson et al. with the method of Kamb in order to achieve the expected advantage of developing a sensitive and diagnostic method for screening a test compound because by incorporating specific mammalian cell types one could target specific human diseases.

Response to arguments:

Applicants’ arguments and amendment with reference to the above rejection have been considered and found not persuasive because first, claim 17 is dependent on Claim 1, which recites HepG2 cell type, thus independent claim 1 must be drawn to or encompasses such limitation. Second, as stated above in the rejection plurality of cells include T-cells, B-cells and astrocyte cells, in addition to Hepatoma cells (see page 27, lines 1-11, page 30, lines 8-10 of the Johnson et al. disclosure). Thus Applicants amendment does not overcome the rejection since Johnson et al. teach cell types that matches with the cell types in the instant claims 1 and 19, and combination of Johnson et al. in view of Kamb renders the rejection obvious. Therefore the rejection is maintained herein.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 1, 2, 6-7, 10-13, 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al. (USPN. 5,985,829).

Harris et al. teach a method of claim 1, 6, and 19, of identifying the function of a test compound (a polypeptide) comprising

(i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43);

(ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20);

(iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67);

wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30 column 10, lines 20-23, column 9, lines 6-7).

With regard to claim 2, and 7, Harris et al. teach that expression of at least two genes or three or more genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, for p53 and helicase gene activity column 6, lines 5-20, for RNA polymerase II or ATPase activity);

With regard to claim 10, Harris et al. teach cell types are provided in a container (culture plates, seeded on cover slips, see column 19, lines 64-67);

With regard to claim 11, expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31);

With regard to claim 12, test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44);

With regard to claim 13, said test compound is a polypeptide (see column 11, lines 18-43);

With regard to claim 15, cell types comprise human cells (see column 19, lines 64-67).
Thus the disclosure of Harris et al. meets the limitations in the instant claims.

B. Claims 1-3, 7, 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Garner (USPN. 6,657,758).

Garner teaches a method of claim 1, of identifying the function of a test compound (UV radiation), wherein the method comprises

(a) providing at least three mammalian cell types which comprise keratinocytes, Langerhans and fibroblast cell types (see column 15, lines 3-11),

(b) contacting each of the cell types with a test compound (irradiation with UV rays) (see column 15, lines 12-22);

(c) measuring expression of one or more genes in each of the cell type (see column 15, lines 20-28), wherein an alteration in the expression of said one or more genes in each type in the presence of a test compound relative to the expression of said one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 17, lines 15-25).

With regard to claims 2-3, and 7, Garner teaches that the method comprises measuring 5 genes in each cell type (see column 15, lines 48-52);

With regard to claim 10, Garner teaches said cell types are provided in a container (see column 15, lines 14-20).

Thus the disclosure of Garner meets the limitations in the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 3 and 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Friend et al. (USPN. 6,303,291).

Harris et al. teach a method of identifying the function of a test compound (a polypeptide) comprising (i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types

comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43); (ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20); (iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67); wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30 column 10, lines 20-23, column 9, lines 6-7).

Harris et al. also teach that (a) expression of at least two genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, column 6, lines 5-20); (b) cell types are provided in a container (culture plates, seeded on cover slips see column 19, lines 64-67); (c) expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31); (d) test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44); (e) said test compound is a polypeptide (see column 11, lines 18-43); (f) cell types comprise human cells (see column 19, lines 64-67).

However, Harris et al. did not teach expression of at least five genes in each cell type, contacting cell types with two or more test compounds.

Friend et al. teach a method for identifying the functions of a drug in a cell type, wherein Friend et al. teach that the method comprises (i) detection of gene expression of 50 genes at a given time (which includes the limitation of claim 3, i.e., expression of at least five genes, see

column 14, lines 50-56); (ii) contacting the cell types with two or more test compounds (column 4, lines 58-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Harris et al. with the method of Friend et al. which is applicable to screen a large number of drug targets using an array system because Friend et al. taught that a faster and less expensive high throughput array system to identify multiple primary targets in cell through which a drug acts on the cell, based on the interpretation of gene expression data(see column 3, lines 1-34). An ordinary practitioner would have been motivated to combine the method of Harris et al. with the high throughput assay system as taught by Friend et al. in order to achieve the expected advantage of developing a high throughput array method for screening a test compound because incorporation of the limitations taught by Friend et al. would reduce cost and time and allows the development of a high-throughput analysis method.

B. Claims 18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Aller (USPN. 6,479,241).

Harris et al. teach a method of identifying the function of a test compound (a polypeptide) comprising (i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43); (ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20); (iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines

20-23, column 2, 43-67); wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7).

Harris et al. also teach that (a) expression of at least two genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, column 6, lines 5-20); (b) cell types are provided in a container (culture plates, seeded on cover slips see column 19, lines 64-67); (c) expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31); (d) test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44); (e) said test compound is a polypeptide (see column 11, lines 18-43); (f) cell types comprise human cells (see column 19, lines 64-67).

However, Harris et al. did not teach measuring expression using real-time polymerase chain reaction.

Aller teaches a high throughput screening assay to identify the function of a test compound wherein Aller teach culturing cells in a microplate along with a test compound and measuring expression of one or more genes using real time PCR (see column 1, lines 63-67, column 2, lines 1-55, column 6, lines 30-60). Aller also teaches use of any cell line which can be cultivated in vitro and specifically cell lines are selected from cells expressing cancer genes, apoptosis, DNA damage or loss of heterozygosity (see column 3, lines 2-15, table-1).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Harris et al. with the method of Aller et al. because Aller taught that the combination of

robotics, standard molecular biology techniques (e.g., cell lysis, RNA isolation, reverse transcription), and real time PCR yields a high-throughput analysis and avoids contamination (see column 2, lines 33-41). An ordinary practitioner would have been motivated to combine the method of Harris et al. with the combination of techniques as taught by Aller in order to achieve the expected advantage of developing a high throughput analysis method for screening a test compound because incorporation of the limitations taught by Aller would reduce contamination and allows the development of a high throughput analysis method.

C. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Johnson et al. (WO 99/37817).

Harris et al. teach a method of identifying the function of a test compound (a polypeptide) comprising (i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43); (ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20); (iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67); wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30column 10, lines 20-23, column 9, lines 6-7).

Harris et al. also teach that (a) expression of at least two genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, column 6, lines 5-20); (b) cell types are provided in a container (culture plates, seeded on cover slips see column

19, lines 64-67); (c) expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31); (d) test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44); (e) said test compound is a polypeptide (see column 11, lines 18-43); (f) cell types comprise human cells (see column 19, lines 64-67). However, Harris et al. did not teach cell types selected from the group according to claim 17.

Johnson et al. teach a method of identifying the function of a test compound, wherein Johnson et al. disclose that the method comprises (i) providing a plurality of cells, the plurality comprising at least two different cell types and exposing the plurality of cells with a test compound (see page 53, lines 1-60; (ii) measuring expression of one or more genes in the said cell types and comparing the expression of said genes with a reference cell and an alteration in said gene expression indicates the function of said test compounds (see page 53, claim 1, lines 7-15, page 11, lines 3-5). Johnson et al. teach that the cell types are selected from a group consisting of HepG2 cells, B-cells, T-cells (jurkat), astrocytes (see page 27, lines 1-11, page 30, lines 8-10); test compound as a polypeptide (see page 54, claim 14); plurality of cell types contacted with two or more test compounds (see page 54, claim 12); and plurality of cells include mammalian cells from human subjects (see page 39, lines 12-19).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Harris et al. with the cell types as taught by Johnson et al. because Johnson et al. taught that “the cell lines that show the largest number of differentially expressed genes were chosen for the study.” (see page 30, lines 14-16). An ordinary practitioner would have been motivated to combine the

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method of Harris et al. with the combination of cell lines as taught by Johnson et al. in order to achieve the expected advantage of developing a sensitive high throughput analysis method for screening a test compound because incorporation of the cell lines as taught by Johnson et al. would enhance the differential expression of genes and improve the sensitivity and specificity of the method.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

SCC
Suryaprabha Chunduru
January 20, 2004

Jehanne Sitten
Primary Examiner
P.
1/21/04